REMARKS

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1, 3-18 and 20-108 are pending in the application. Claims 2 and 19 have been cancelled. These changes do not introduce new matter, and their entry is respectfully requested.

In the Office Action of February 27, 2002, the Examiner set forth a number of grounds for rejection. These grounds are addressed individually and in detail below.

Election/Restriction

Applicants acknowledge that the Examiner has made the restriction final and, withdrawn claims 65-108 from consideration. Applicants elect claims 1-64 to continue prosecution.

Objections to the Specification

1. Title

The title of the invention stands objected to as not being descriptive. The Examiner has requested a new title to clearly indicate the invention.

In response, Applicants have amended the title to read: A BIOLOGICAL ASSAY METHOD".

2. The specification

The Examiner objects the specification for the reasons set forth on page 2 of the Outstanding Office Action. Applicants have deleted the word "specification" in paragraphs 1 and 2 on page 3 of the specification.

Accordingly, it is believed this ground of objection has been obviated, and may properly be withdrawn.

Rejections Under 35 U.S.C. §102

Claims 1, 5-17, 20, 22 and 24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Li for the reasons set forth on pages 2-3 of the Outstanding Office Action.

Applicants have amended the independent claim 1 to include the limitation of claim 2. That is ". . . a biochip in the form of an elongate enclosed microchannel with an internal bore; . . .". Claims 5-17, 20, 22 and 24 depend on claim 1. Accordingly, Applicants respectfully traverse the rejection. For anticipation under 35 U.S.C. §102, the reference "must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." (MPEP §706.02, Rejection on Prior Art [R-1]). The Federal Circuit has held that prior art is anticipatory only if every element of the claimed invention is disclosed in a single item of prior art in the form literally defined in the claim *(Jamesbury Corp. v. Litton Indus.*

Products, 756 F.2d 1556, 225 USPQ 253 (Fed. Cir. 1985); *Atlas Powder Co. v. du Pout*; 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); *American Hospital Suppl v. Travenol Labs*, 745 F.2d 1, 223 USPQ 577 9Fed. Cir. 1984).

Li discloses the use of electro-osmotic and/or electrophoretic pumping to drive cell transport in a network of capillary channels fabricated on a glass chip. The direction of cell flow can be controlled by applying different electrical potentials at each end of the capillary channel. Li does not disclose the biochip in the form of an elongated enclosed microchannel with an internal bore.

Thus, the present invention is distinguishable from the Li reference. These grounds of rejection have been obviated and thus, withdrawal of each of the outstanding 35 U.S.C. §102 rejections is respectfully requested.

Rejections Under 35 U.S.C. §103

Claims 2-4, 18, 19, 21, 23 and 25 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Li for the reasons set forth on page 4 of the Outstanding Office Action.

Applicants have canceled claims 2 and 19. Claims 3-4 have been amended to include functional language ". . . to study cell attachments" and ". . . to study cell-cell interaction". Accordingly, Applicants respectfully traverse the rejection. To establish a prima facie case of obviousness of a claimed invention,

all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patenability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

The present invention provides a biological assay method and a biological assay apparatus with an elaborate channel design. The present invention further discloses the use of biochip to study cell adhesion or cell migration to chemoattractants.

In contrast, Li discloses the use of electro osmotic and/or electrophoretic pumping to drive cell transport in a network of capillary channels fabricated on a glass chip. Because the cells are negatively charged and migrated in the direction of the anode, their movement in a capillary channel can be controlled by applying different electrical potentials at each end of the capillary channel. Li's study was focused on the control of cell flow by electrical field. Li does not teach or suggest cell-cell/cell-ligand interactions or the active swimming of cells towards chemoattractants. Additionally, Li does not disclose the elaborate channel designed of the present invention that facilitates cells interactive and movement in microchannels with internal bores.

Furthermore, Li uses electrokinetic effects to control cell movement in a microfluidic system, which is different from the syringe pump controlled cell movements of the present invention. The AquaSil coating described by Li is intended to facilitate cell movement, while the protein or cell coating of the present invention

is used for testing cell attachment. Although Li tested several cell types, it does not teach or suggest the separation of one cell type from the others by the microfluidic system. Therefore, the Li reference is directed to a different use of microchannel. One skilled in the art would not be able to produce the present invention based on Li without undue experimentation.

The Examiner also indicates that the function of chemoattractants is well known in the art. The Examiner's contention is respectfully traversed. Li neither mentions anything about chemoattractants, nor discloses anything remotely related to an assay of cell migration to chemoattractants. Beyond mere conclusory statements, there is no prior art reference cited to support the Examiner's position. The mere allegation that the differences between the claimed subject matter and the prior art are obvious does not create a presumption of unpatentability which forces an applicant to prove conclusively that the USPTO is wrong. *In re Soli, 317 F.2d 941 (CCPA 19623).* The ultimate legal conclusion of obviousness must be based on facts or records and subjective opinions are of little weight against contrary evidence. *In re Wagner et al. 371 F.2d 877 (CCPA 1967).*

Taken together, the Examiner has not met the burden to establish a *prima facie* evidence of obviousness. This ground of rejection has been obviated and thus, withdrawal of 35 U.S.C. §103 rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 2-64 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth on page 5 of the Office Action.

Applicants have complied with the Examiner's suggestion and amended claims 3-18 and 20-64. Claims 2 and 19 have been canceled.

These grounds of rejection have been obviated, and may properly be withdrawn.

Accordingly, in view of the above amendments and remarks, reconsideration of the rejections and allowance of the claims of the present application are respectfully requested.

CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the

Examiner is invited to contact Ping Wang, M.D. (Reg. No. 48,328) at the Office of Birch, Stewart, Kolasch & Birch, LLP.

Prompt and favorable consideration of this Response is respectfully requested.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three-month extension of time for filing a reply in connection with the present application, and the required fee of $460.00 is attached hereto.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Joseph A. Kolasch, Reg. No. 22,463

JAK/PW/end
1817-0105P

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE TITLE:

The title has been amended as follows:

A BIOLOGICAL [ASSAYS] ASSAY METHOD

IN THE SPECIFICATION:

The paragraph beginning on page 3, line 7, has been amended as follows:

The most commonly used cell transmigration assay is a modified "Boyden chamber" assay such as described in US Patent [Specification] No. 5578492 (Fedun et al). This involves assessing the crossing of a quantity of cells through a microporous membrane under the influence of a chemoattractant, recombinant or cell-derived. Here the diameter of the micropores are less than the diameter of the cells under investigation, such that the cells must deform themselves in order to squeeze through the pores thereby constructing an analogy to the transendothelial migration of cells in physiological circumstances. Once the cells are deposited onto the membrane, the chamber can be incubated for intervals over time at a suitable temperature, usually 37°. Following this, the bottom chamber or opposite side of the top chamber may be [analysed] analyzed for cells that have squeezed through the microporous membrane.

The paragraph beginning on page 3, line 19, has been amended as follows:

US Patent [Specification] Nos. 4912057 (Guirguis et al), 5284753 (Goodwin et al), 5302515 (Goodwin et al), 5514555 (Springer et al) and 5601997 (Tchao) are typical examples of these assays. The main disadvantage of the assays described in those specifications is that the biological process of transmigration through the micropores is difficult to observe due to the geometrical configuration of the apparatus involved. The lens of the optically inverted microscope must be able to focus through the lower chamber and the microporous membrane. This obviously leads to difficulties due to optical aberrations. In effect, the study of the cells morphology changes while transmigrating across the membrane and their subsequent cytoskeletal changes reverting to their former state is a process which is difficult to monitor and record due to limitations with current techniques. In addition, although it is possible to alter such an experiments parameters following the initiation of the experiment, such as the introduction of a second chemoattractant, recombinant or cell-derived, at some specified time after commencing the experiment, it is not possible to distinguish separate effects from each said chemoattractant.